UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/090,516	03/01/2002	Xuanchuan Yu	LEX-0316-USA	6467

24231 7590 06/16/2004

LEXICON GENETICS INCORPORATED
8800 TECHNOLOGY FOREST PLACE
THE WOODLANDS, TX 77381-1160

EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	10/090,516	YU ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 14 May 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *14 May 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see attachment*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☐ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *1,3-5 and 9-13*.

Claim(s) withdrawn from consideration: _____.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

ADVISORY ACTION

[1] Applicants' request for reconsideration, filed May 14, 2004, is acknowledged. However, applicants' response does not place the application in condition for allowance for the reasons stated below. No claims have been amended in applicants' response.

[2] The rejection of claims 1, 3-5, and 9-13 under 35 USC § 101 and the corresponding enablement rejection of claims 1, 3-5, and 9-13 under 35 USC § 112, first paragraph, are maintained for the reasons of record as set forth in items [8] and [9] of the Office action mailed January 09, 2004 and for the reasons stated below.

[3] RESPONSE TO ARGUMENTS: Beginning at the top of page 2 of the response, applicants argue the invention has a number of substantial and credible utilities such as using the disclosed polymorphisms in forensic biology, which is an asserted "real world" utility. Applicants argue the polymorphisms can be used to distinguish members of the human population from one another based on the presence or absence of the disclosed polymorphism. Applicants allege the disclosed polymorphism can be used in a manner similar to other polymorphic markers in forensic biology, which is allegedly a well-established technique whose methodology need not be disclosed in the specification. Applicants argue that at worst the polymorphisms are useful for distinguishing 50% of the population, which is allegedly a "real world" use. Applicants assert various situations wherein the disclosed polymorphisms are allegedly useful. Applicants' arguments are not found persuasive.

The examiner maintains the position that the specification fails to assert a substantial and specific utility for the claimed invention and there is no well-established

use for the claimed invention, particularly in forensic analysis. It should be noted that the claims are drawn to the nucleic acid of SEQ ID NO:1 and not to the polymorphism(s) themselves and thus the issue is whether the claimed nucleic acid has utility – not the disclosed polymorphism(s). See MPEP 2107.02, which states, "[t]he claimed invention is the focus of the assessment of whether an applicant has satisfied the utility requirement." It should also be noted that, contrary to applicants' arguments, there is no evidence of record that would indicate that the claimed nucleic acid is useful for forensic analysis. Applicants cite the examples of using polymorphisms to include/exclude a criminal suspect, identify human remains, or in paternity determination. However, without knowing the occurrence of the disclosed polymorphism, one of ordinary skill in the art clearly would not use such a polymorphism for purposes of identification. For example, if the polymorphism occurred in 100% of the male population, how is it so useful in paternity determination? Or if the polymorphism was so rare that it occurred only once out of every one billion subjects. Clearly such a polymorphism would not be useful for including/excluding a criminal suspect or identifying human remains. As such, one of ordinary skill in the art would recognize that additional research is required to identify a "real world" use for the claimed invention and consequently, the claimed nucleic acid has no substantial utility. While not expressly stated by applicants, it would appear that the asserted specific and substantial use of the claimed nucleic acid of SEQ ID NO:1 is to assay for itself or the disclosed variants of SEQ ID NO:1, i.e., "forensic analysis." Providing an example of a utility that is not specific, MPEP 2107.01 states, "[a] method of assaying for or identifying a material that itself has no specific and/or

substantial utility." As the claimed nucleic acid of SEQ ID NO:1 and disclosed variants thereof have no specific and substantial asserted utility, it follows that the use of assaying for the same is not a substantial utility.

Beginning at the middle of page 4 of the response, applicants argue the examiner has not stated the proper standard for meeting the requirements of 35 USC 101, which is not whether additional experimentation is required, but whether undue experimentation would be required to practice the claimed invention. Applicants argue that the widespread use of polymorphisms argues against this use as requiring undue experimentation. Applicants' argument is not found persuasive.

Contrary to applicants' assertion, the examiner has applied the proper standard for meeting the substantial requirement of 35 USC 101. MPEP 2107.01 states, "[u]tilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities." See, e.g., *Brenner v. Manson*, 383 U.S. 519, 534-35, 148 USPQ 689, 695 (1966). In this case, the asserted utilities require further research to identify a "real world" context of use and consequently are not substantial utilities.

Beginning at the top of page 5 of the response, applicants argue the asserted utilities are specific because not all nucleic acids contain polymorphic markers. Applicants argue the examiner uses an improper hindsight verification that the claimed sequence would be expected to have polymorphic markers and further argue the examiner has confused the requirement for a specific utility with the requirement for a unique utility. Applicants' argument is not found persuasive.

It is again noted that the claims are drawn to the nucleic acid of SEQ ID NO:1 and not to the polymorphism(s) themselves and thus the issue is whether the claimed nucleic acid has utility – not the disclosed polymorphism(s). Contrary to applicants' argument, the examiner has only required an asserted use that is specific – not unique – to the claimed invention. It would appear that applicants argue that the asserted utility of the nucleic acid of SEQ ID NO:1 is to assay for itself or the disclosed variants of SEQ ID NO:1, i.e., "forensic analysis." Regardless of whether variants of the claimed nucleic acid exist, the use of the claimed nucleic acid as a detection reagent, e.g., as a hybridization probe, applies to the broad, general class of nucleic acids. Alternatively stated, any nucleic acid can be used as a hybridization probe. As applicants have failed to correlate the claimed nucleic acid with any particular phenotype, e.g., a disease state, this use is not specific. In this case applicants merely indicate that the invention may prove useful without identifying with specificity why it is considered useful. Consequently, the claimed nucleic acid has no specific utility.

Beginning at the top of page 7 of the response, applicants argue the polymorphism is included in the claimed nucleic acid and one of the asserted utilities is the use of the polymorphism in forensic analysis. Applicants argue that only one credible utility is need to satisfy 35 USC 101. Applicants assert the examiner's arguments regarding the lack of guidance in the specification and that further experimentation is required to establish a "real world" use have been overcome and that

none of the examiner's arguments regarding forensic analysis support the lack of unity. Applicants' arguments are not found persuasive.

It is again noted that the claims are drawn to the nucleic acid of SEQ ID NO:1 and not to the polymorphism(s) themselves and thus the issue is whether the claimed nucleic acid has utility – not the disclosed polymorphism(s). Applicants argue that the polymorphism is "included" in the claimed nucleic acid. However, regardless of whether SEQ ID NO:1 is considered to be a "wild-type" or polymorphic sequence, it remains that the claimed sequence has no specific and substantial asserted utility at least for the reasons of record and the reasons stated above. In this case, the specification fails to assert even a single specific and substantial utility. Regarding applicants allegation that the examiner's arguments have been overcome, contrary to applicants' assertion, none of the examiner's arguments have been overcome – particularly those arguments addressing forensic analysis.

Beginning at the bottom of page 7 of the response, applicants argue that a statement of utility must be accepted absent reasons why one skilled in the art would have reasons to doubt the objective truth. Applicants argue the holding of In re Langer was directed to the "the utility requirement of § 101", disputing the examiner's assertion that the holding of In re Langer was directed to the credibility of an asserted utility. Applicants argue that unless the examiner can provide evidence that the disclosed polymorphism cannot be used in forensic analysis, applicants' asserted utility must be taken to satisfy the utility requirement of 35 USC § 101, citing MPEP § 2100 as evidence thereof. Applicants' argument is not found persuasive.

It is again noted that the claims are drawn to the nucleic acid of SEQ ID NO:1 and not to the polymorphism(s) themselves and thus the issue is whether the claimed nucleic acid has utility – not the disclosed polymorphism(s). The examiner maintains the position that this quote of Langer appears to address the issue of credibility of an asserted utility at least for the following reasons. First, it is noted that applicants' cited quotes taken from the MPEP and In re Langer are cited in the MPEP under the section addressing evaluation of the *credibility* of an asserted utility. See MPEP 2107.02. Second, MPEP 2107.02 states, "[t]hus, Langer and subsequent cases direct the Office to presume that a statement of utility made by an applicant is true," and this statement clearly addresses the *credibility* of an asserted utility. And third, nowhere in the MPEP is the examiner directed to evaluate the asserted utility of a claimed invention based only on its credibility. To the contrary, MPEP 2107.02 states, "[a] complete disclosure should include a statement which identifies a specific and substantial utility for the invention."

In this case, it appears that applicants argue that all that is needed to satisfy the utility requirement of 35 USC § 101 is that the asserted utility is credible. However, as stated above, "[a] complete disclosure should include a statement which identifies a specific and substantial utility for the invention." See MPEP 2107.01 and 2107.02. In accordance with MPEP 2100 and the holding of Langer, the examiner has evaluated applicants' asserted utilities and determined that they are credible. However, it is the examiner's position that the asserted utilities are not specific and substantial at least for the reasons of record and the reasons stated above.

Beginning at the middle of page 8 of the response, applicants assert the examiner's "tortured logic borders on the absurb", citing quotes from the Office action which state, "applicants' assertion that the claimed sequence is a human Ten-m4 protein variant is acknowledged" and "there is no assertion that the proteins of SEQ ID NO:2 and 4 have Ten-m4/cdz activity." Applicants argue that the title of the specification, i.e., "Novel Human TEN-M4/cdz Proteins and Polynucleotides Encoding Same" is an assertion that the claimed invention encodes a polypeptide having Ten-m4/cdz activity. Applicants' argument is not found persuasive.

Regarding applicants' assertion that the examiner's "tortured logic borders on the absurd," applicants are reminded that "[a]pplicants and their attorneys or agents are required to conduct their business with the Patent and Trademark Office with decorum and courtesy." See 37 CFR 1.3. Addressing the merits of the argument, it is noted that there is no inconsistency in the examiner's statements. In the first quote, the examiner merely acknowledged an assertion that the claimed sequence encodes a TEN-M4/cdz protein *variant*, i.e., a protein with structural similarity to a TEN-M4/cdz protein. The second quote makes clear that the specification fails to assert that the claimed sequences encode proteins with TEN-N4/cdz biological activity, i.e., a protein sharing the same function. Not all variants of a protein share its function, e.g., an inactive variant, and thus, the two statements are not inconsistent. The examiner maintains the position that the specification has failed to expressly assert that the claimed nucleic acid encodes a polypeptide having Ten-m4/cdz activity, whatever that may be as the specification and the prior art fail to define such an activity. One of skill in the art would

recognize that this title can just as well be directed to a biologically inactive polypeptide, i.e., a polypeptide that would be void of Ten-m4/cdz activity. It should be noted that structural similarity or similarities alone cannot be used to differentiate between a biologically active or inactive polypeptide.

Beginning at the top of page 9 of the response, applicants argue that the examiner's assertion that "only by empirical characterization can the function of a protein be ascertained" is inconsistent with legal precedent, knowledge of the skilled artisan, and USPTO policy. Applicants arguments are not found persuasive.

It should be noted that, contrary to applicants' assertion, the examiner's statement that "only by empirical characterization can the function of a protein be ascertained," is supported by the prior art references of Brenner and Scott et al. In this case, there is no dispute that functional prediction based on sequence similarity or similarities is a powerful tool. However, as evidenced by at least Brenner and Scott et al., such methods are limited to prediction of a polypeptide's function and cannot be used to confirm a polypeptide's function, which requires empirical evidence. As a skilled artisan would recognize that without such evidence at the time of the invention, the polypeptide encoded by the claimed invention can just as likely be a non-functional polypeptide. Regarding applicants' reference to the Revised Interim Utility Guidelines, it is noted that the "specification" of Example 10 makes an assertion that "SEQ ID NO: 2 encodes a DNA ligase" (see "Analysis" section of Example 10), i.e., the specification asserts the claimed nucleic acid encodes a polypeptide having a particular function. However, in this case, no such assertion has been made.

At the top of page 10 of the response, applicants attempt to define "Ten-m4/cdz activity" by arguing that the role of Ten-m4/cdz proteins has been known for a number of years, citing Levine et al. and Ben-Zur et al. At the middle of page 10 of the response, applicants argue that the reference of Feng et al., which was published after the filing of the instant application, is evidence that other skilled artisans have confirmed applicants' assertion that the claimed Ten-m4/cdz sequence has a role in development. At the bottom of page 10 of the response, applicants argue that given the alleged well-established role of Ten-m4/cdz proteins in development, one of ordinary skill would readily understand the biological significance of the claimed invention, which is its involvement in development. Applicants' arguments are not found persuasive.

It should be noted that neither of the references of Levine et al. or Ben-Zur et al. addresses a Ten-m4/cdz protein and instead address proteins referred to as "odz" or "Tenm." It is unclear from the prior art and the specification as to whether a Tenm and/or an odz protein as described by Levine et al. and Ben-Zur et al. is/are the same as a Ten-m4/cdz protein. Although these references may indicate that odz and Tenm have an unidentified and undefined role in developmental patterning, the references are silent as to the specific biological activity or biological significance of odz and Tenm. Even assuming arguendo that one of skill would have been able to recognize that the "role" of Ten-m4/cdz is in developmental patterning, this says nothing about the specific biological activity or significance of Ten-m4/cdz such that a skilled artisan would have been able to use the claimed invention in its currently available form. Regardless of

whether the protein encoded by SEQ ID NO:1 and 3 has a role in development, this alleged "biological activity" is little more than an assertion that the protein has useful biological properties. In this case, applicants merely indicate that the invention may prove useful as having a role in development without identifying with specificity why it is considered useful.

Addressing the reference of Feng et al., although Feng et al. may provide evidence that Ten-m4 has some unidentified and undefined role in development, this reference was not available at the time of the invention and, as a skilled artisan would not have recognized the proteins of Levine et al. and Ben-Zur et al. as being Ten-m4/cdz proteins, one would not have recognized that Ten-m4/cdz may have a role in developmental patterning. Further, as stated above, even assuming arguendo that one of skill would have able to recognize that the "role" of Ten-m4/cdz is in developmental patterning, this says nothing about the actual biological activity or biological significance of Ten-m4/cdz such that a skilled artisan would have been able to use the claimed invention in its currently available form. In this case, applicants merely indicate that the invention may prove useful as having a role in development without identifying with specificity why it is considered useful.

At the top of page 11 of the response, applicants argue that, given the alleged known involvement of Ten-m4/cdz proteins in development, a skilled artisan would appreciate the use of the claimed sequence for tracking its expression. Applicants argue that since the sequences are markers of human chromosome 11, a skilled artisan would recognize the claimed sequences would be an "ideal, novel candidate" for use in gene

expression analysis with DNA chips. Applicants argue that due to the widespread utility of gene chips using public domain gene information, there can be little doubt that the claimed sequences would have utility in DNA chip applications and that compositions that enhance the utility of such DNA chips must themselves be useful. Beginning at the middle of page 11 of the response, applicants argue that evidence of "real world" substantial utility, is further provided by the fact that there is an entire industry established based on the use of gene sequences in DNA chip format. Applicants argue that the use of gene sequences is a "real world" substantial, widespread and well-established utility. Applicants argue that the utility of genomic data, and specifically human genomic data is well recognized, citing Venter et al. and Jasny et al. as allegedly supporting their argument. Applicants' arguments are not found persuasive.

Regarding the asserted utility of the claimed sequences in gene expression monitoring using gene chips, it is noted that any sequence can be included as a component of a gene chip, e.g., as a chromosomal marker. This utility is not specific to the claimed sequences and instead applies to the general class of nucleic acids as evidence by applicants' own statement regarding the widespread use of such gene chips using public domain gene sequences. It is also noted that the claims are drawn to polynucleotide sequences – not to the physical DNA chip itself or methods of use thereof. Furthermore, any information derived from gene expression analysis using the claimed sequences would be meaningless as the specification fails to provide guidance for interpreting any result obtained thereby.

Addressing applicants' argument of the widespread use of gene chips, evidence of commercial success, while sometimes persuasive as secondary evidence of non-obviousness, is immaterial to utility and enablement. Many products have enjoyed commercial success due to fads or clever advertising, wherein the products would not have met the legal standards for utility under 35 USC § 101. In this case, there is no dispute as to the potential usefulness of information obtained from the sequencing of the human genome. However this information is valuable to the extent that it provides a starting point for scientists to further investigate the biological significance of the genetic information collected. In the absence of any information as to the interpretation of a result obtained by gene expression analysis using a DNA chip, the claimed sequences are useful only for further experimentation to investigate their biological significance. As such, the asserted utility of gene expression analysis is not a substantial utility. It should be noted that the issue at hand is the utility of the claimed sequences and not DNA chips or methods of use thereof. In the instant case, applicants have failed to demonstrate a patentable utility for the claimed invention.

At the top of page 12 of the response, applicants argue that the lack of 100% consensus on the role of Ten-m4/cdz proteins in development is irrelevant to the question of whether the asserted utility is specific and substantial. Applicants argue that the legal test for utility involves an assessment of whether those of skill in the art would find any of the utilities described for the invention to be believable and assert that in view of the references of Levine et al., Ben-Zur et al., and Feng et al., one of skill would believe that Ten-m4/cdz proteins have a role in development. Applicants assert

believability is the standard for meeting the requirement of 35 USC 101. Applicants' arguments are not found persuasive.

As stated above, while the prior art may indicate that "Tenm" and "odz" proteins are involved in development, neither the specification nor the prior art provides any indication that the claimed sequence is involved in development, thus one would not recognize its role as such. Also, even assuming arguendo the prior art and/or the specification asserted such a role, this is no indication as to the encoded protein's biological activity or its biological significance such that one of skill in the art could use the protein in its currently available form without further experimentation to identify a "real-world" use for the claimed nucleic acid. Regardless of whether the protein encoded by SEQ ID NO:1 and 3 has a role in development, this alleged "biological activity" is little more than an assertion that the protein has useful biological properties. In this case, applicants merely indicate that the invention may prove useful as having a role in development without identifying with specificity why it is considered useful. The legal standard for utility is that the claimed invention has a specific, substantial, and credible asserted utility or a well-established utility. In this case, the credibility (or believability) of the asserted utility is not at issue as there is no dispute that the claimed nucleic acids can be used, inter alia, to track gene expression or to identify a polymorphism. However, at least for the reasons of record and for the reasons stated above, the claimed invention has no specific and substantial asserted utility.

Beginning at the middle of page 12 of the response, applicants argue the examiner's assertion that the use of sequences in gene expression monitoring is flawed

in three respects: 1) only expressed sequences can be used to track gene expression; 2) the claimed sequence is involved in development, which distinguishes it from "any sequence" and expression profiling does not require knowledge of the function of a nucleic acid; and 3) applicants reiterate their argument that the examiner has confused the requirements for a specific utility with a unique utility. Applicants' arguments are not found persuasive.

Addressing argument 1), the asserted utility of using the claimed sequences for gene expression monitoring is neither specific nor substantial. All nucleic acids, whether expressed or non-expressed, can be used for gene expression monitoring and consequently this utility is not specific. Moreover, this utility is not substantial as any information provided by gene expression analysis is meaningless as the specification fails to provide any guidance as to how one would interpret data obtained from such an analysis.

Regarding argument 2), while the prior art may indicate that "Tenm" and "odz" proteins are involved in development, neither the specification nor the prior art provides any indication that the claimed sequence is involved in development, thus one would not recognize its role as such. Also, even assuming arguendo the prior art and/or the specification asserted such a role, use of the claimed sequence for expression profiling is not specific as stated above as all nucleic acids can be used for such use. Moreover, there is no indication as to the encoded protein's biological activity or its biological significance. Thus, further experimentation to interpret the results of any gene expression monitoring using the claimed nucleic acids.

Regarding argument 3), as stated above, any nucleic acid can be used in gene expression monitoring, and consequently, this utility is not specific. Applicants mischaracterize the examiner's position as applicants have only been required to identify a utility that is specific to the invention claimed.

At the middle of page 13 of the response, applicants argue that one would be able to interpret the results obtained from gene expression monitoring, given the alleged well-established role of Ten-m4/cdz proteins in development. Applicants argue that guidance for interpreting the results of gene expression monitoring is not required as a large industry has been established based on the use of gene sequences for expression monitoring and applicant need not disclose what is well known in the art. Applicants' argument is not found persuasive.

It is noted that, as stated above, neither the prior art nor the specification provides any evidence that the claimed nucleic acid has any role in development and more specifically, what this role may be, i.e., the specific biological activity or biological significance of the claimed sequence. Even assuming arguendo the prior art and/or the specification asserted such a "role" in development, this is no indication as to the encoded protein's biological activity or its biological significance such that one of skill in the art could use the protein in its currently available form without further experimentation to identify a "real-world" use for the claimed nucleic acid. Regardless of whether the protein encoded by SEQ ID NO:1 and 3 has a role in development, this alleged "biological activity" is little more than an assertion that the protein has useful biological properties. In this case, applicants merely indicate that the invention may

prove useful as having a role in development without identifying with specificity why it is considered useful. There is no evidence of the biological significance of the claimed nucleic acid at the time of the invention. Evidence that a particular nucleic acid has increased, decreased, or the same expression during development is of little use without knowledge of its biological significance, which has not been determined in this case. Consequently, this asserted utility is not substantial as the specification fails to provide guidance for interpreting the results obtained thereby. It should be noted that the establishment of an industry based on the use of gene chips for expression monitoring provides no guidance for interpreting the results of expression monitoring of the claimed nucleic acid.

Beginning at the bottom of page 13 of the response, applicants argue that contrary to the examiner's assertion, evidence of commercial success of gene chips is direct evidence that the claimed nucleic acid has a "real world" context of use in its currently available form. Applicants' argument is not found persuasive.

In this case, there is no evidence of record that would indicate that *the claimed sequences* enjoy commercial success and/or that *the claimed sequences* are commercially desirable as components of a gene chip for gene expression monitoring or that a gene chip *comprising the claimed nucleic acids* is any more commercially successful or valuable than any other gene chip. Even assuming arguendo such evidence were made of record, it is noted that the specification fails to provide guidance that would enable a skilled artisan to interpret the use of the results of gene expression monitoring using the claimed nucleic acid. Further, the claimed nucleic acid can be used

for gene expression monitoring – just as any other nucleic acid. Consequently, this utility is neither specific nor substantial.

At the top of page 14 of the response, applicants argue that non-expressed sequences cannot be used to monitor gene expression and request the examiner to provide evidence to support the examiner's position. Applicants argue that without such evidence, the examiner's argument fails to support the instant rejection. Applicants' argument is not found persuasive.

It is noted that the use of a non-expressed nucleic acid, i.e., a nucleic acid that is not transcribed, for gene expression monitoring can certainly be practiced. Although a nucleic acid may not be expressed, this in itself does not preclude the use of a non-expressed nucleic acid for being used in gene expression monitoring. What is being monitored is "expressed genes" and what is used to conduct the monitoring does not necessarily have to be expressed at all. Many nucleic acids can be used as probes for expressed genes that are not themselves expressed, e.g., fragments, variants, and pseudo-genes. Hybridization does not require 100% identity between the probe and its target and thus, the probe does not have to an expressed polynucleotide. It should be noted that, while the examiner has provided no evidence to support this position, applicants have provided no evidence to support their position, i.e., that a non-expressed nucleic acid cannot be used for gene expression analysis, and applicants are reminded that "arguments of counsel alone cannot take the place of evidence in the record." See MPEP 716.01(c).

Beginning at the bottom of page 14 of the response applicants argue the claimed invention has a specific utility in identifying coding sequence and chromosomal mapping. Applicants cite GenBank Accession Numbers AP002515, AP002768, and AP002957 as "show[ing] that the human gene corresponding to the presently claimed sequence is dispersed on 28 exons of human chromosome 11". Applicants argue that since only a minor portion of the genome contains exons, the claimed polynucleotides provide biologically validated empirical data that specifically define that portion of the genomic locus that actually contains an exon and that the claimed polynucleotides define how exons are spliced to produce an active transcript. Applicants argue that since their polynucleotides define biologically validated empirical data, the present claims meet the requirements of 35 USC §101. In applicants' opinion, the claimed sequences provide "exquisite specificity" in localizing the specific region of human chromosome 11 and that this specificity is useful because it is allegedly shared by virtually no other sequences. Applicants reiterate their argument that the examiner has confused the requirements for a specific utility with a unique utility. Applicants' argument is not found persuasive.

As stated above, any expressed human polynucleotide, e.g., a cDNA, can be used to detect a particular locus of the corresponding gene, therefore any human polynucleotide which encodes a protein can be used to determine the specific chromosome which contains that locus and thus, the asserted utility is not specific. Regarding identification of a specific region of human chromosome 11 using the claimed sequences, it is noted that the specification discloses, "[t]he gene encoding the

described NHPs is apparently encoded on one or more of human chromosomes 10 and 11 (see GENBANK accession numbers AC084775 and AP002515)" (page 18, bottom). It should be noted that the specification fails to cite GenBank Accession Numbers AP002768 and AP002957. Thus, contrary to applicants' assertion, the specification merely suggests that the corresponding gene is "apparently encoded" by a nucleic acid sequence present on either chromosome 10 OR chromosome 11. This is far from a "show[ing] that the human gene corresponding to the presently claimed sequence is dispersed on 28 exons of human chromosome 11." In this case, at the time of filing of the instant application, there was no evidence of record or line of reasoning to suggest that the claimed sequences were useful for identifying any specific region of chromosome 11 or that the region comprising the claimed sequences was not shared by other nucleic acids. In this case, in view of the lack of guidance provided in the specification, further research would have been required for a skilled artisan to determine whether the claimed sequences were useful for identifying any specific region of chromosome 11. Applicants are reminded that MPEP 2164.05(a) makes clear that the specification must be enabling as of the filing date of the application. Consequently, the asserted utility is not substantial.

Regarding a unique utility, applicants mischaracterize the examiner's position as applicants have been required to identify a utility that is specific to the invention claimed, as opposed to one that would apply regardless of the specific properties of the claimed invention. An invention certainly can have a utility that is shared by other compounds or compositions. On the other hand, not every utility will satisfy 35 USC § 101, even if the

utility is shared by a class of inventions. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101. Here, applicants assert that the claimed polynucleotides can be used to identify coding sequence and in mapping a unique gene to a particular chromosome. However, there is no indication in the specification that the claimed sequences are specific to chromosome 11, particularly in view of the disclosure of the specification that "[t]he gene encoding the described NHPs is apparently encoded on one or more of human chromosomes 10 and 11." Furthermore, in view of this disclosure, for a skilled artisan to determine whether such specificity for chromosome 11 exists, further research is required. As the asserted utilities are neither specific nor substantial for the reasons of record and the reasons stated above, the claimed invention has no specific and substantial asserted utility.

At the top of page 17 of the response, applicants argue that the Federal Circuit in Juicy Whip Inc. v. Orange Bang, Inc. has stated that the threshold of utility is not high and that an invention is useful under § 101 if it is capable of providing some identifiable benefit. Applicants further cite Brooktree Corp. v. Advanced Micro Devices, Inc. to indicate that the Federal Circuit has stated that a claimed device must be totally incapable of achieving a useful result to lack utility under 35 USC § 101. Applicants cite Cross v. Iizuka in support of their argument that any utility for a claimed invention is sufficient to satisfy the requirements of 35 USC § 101 and indicate that the Federal Circuit has confirmed that anything "under the sun" made by man is patentable in State Street Bank & Trust Co. v. Signature Financial Group, Inc. Applicants argue the

examiner discounts the cited case law that is mandatory legal authority whose precedents must be followed by the examiner. Applicants argue that 35 USC 101 makes no distinction between that which is claimed. Applicants' argument is not found persuasive.

To the extent applicants' arguments address the issue of credibility of an asserted utility, it is noted that the examiner has not questioned the credibility of applicants' asserted use of the claimed polynucleotides. Instead, it is the examiner's position that the specification provides no specific and substantial asserted utility for the claimed invention. It is noted that *Cross v. Iizuka* is considered most relevant to the instant discussion since the inventions in that case are chemical compounds. In *Juicy Whip Inc. v. Orange Bang, Inc.*, the issue of utility was discussed in regard to a juice dispenser, in *Brooktree Corp. v. Advanced Micro Devices, Inc.*, the issue of utility was discussed in regard to digital analog conversion circuitry, and in *State Street Bank & Trust Co. v. Signature Financial Group, Inc.*, the issue of utility was discussed in regard to a business method. As stated above, the claimed invention has no specific and substantial utility as the asserted utilities are applicable to the broad class of polynucleotides and/or require further experimentation to identify a "real world" use. It should be noted that in *Cross v Iizuka*, the specification disclosed the structure of the claimed imidazole derivative compounds and the specification provided experimental evidence of inhibition of thromboxane synthetase inhibition by these imidazole derivatives in human and bovine microsomes and a method for practicing such. In the instant case, the specification fails to provide guidance for practicing <u>any</u> patentable

utility of the claimed sequences – particularly forensic analysis, assessing gene expression patterns using gene chips, and in mapping protein coding regions of chromosomes. Thus, in contrast to *Cross v Iizuka,* the claimed invention fails to benefit the public in currently available form for the reasons of record and the reasons discussed above – particularly for the utilities of forensic analysis, assessing gene expression patterns using gene chips, and in mapping protein coding regions of chromosomes.

It is noted that, contrary to applicants' assertion, the examiner has not discounted the cited case law. The examiner has fully considered applicants' arguments in accordance with MPEP 707.07(f). Instead, the examiner has identified case law that is most relevant to the instant claims, i.e., the utility of claims drawn to chemical compounds. Even assuming that Juicy Whip Inc. v. Orange Bang, Inc., Brooktree Corp. v. Advanced Micro Devices, Inc., Cross v. Iizuka, and State Street Bank & Trust Co. v. Signature Financial Group, Inc. are relevant to the instant rejection, it is noted that the instant rejection does not contradict the cited case law.

Applicants assert the requirements set forth in the Office action for compliance with 35 USC § 101 do not comply with the requirements set forth by the PTO itself for complying with 35 USC § 101. Applicants state that, while they are aware of the new utility guidelines set forth by the USPTO, the current rules and regulations are the patent laws set forth in 35 USC and the rules set forth in 37 CFR but not the MPEP or guidelines set forth by the USPTO. Applicants argue it is the job of the judiciary and not the USPTO to interpret these laws and rules. Applicants argue that they are unaware of

recent changes in either 35 USC § 101 or in the interpretation of 35 USC § 101 by the Supreme Court or the Federal Circuit which support the new utility guidelines set forth by the USPTO. Applicants cite patents that allegedly do not contain examples of the "real world" utilities allegedly required by the Examiner. Applicants argue that holding them to a different standard of utility would be arbitrary and capricious. Applicants argue that the guidelines followed by the USPTO should not be confused with the force of law. Applicants argue there are numerous examples of USPTO guidelines that have been found not to comport with the patent laws and rules and cite *In re Brana* as an alleged example of the Federal Circuit overturning USPTO-enacted guidelines.

Applicants are respectfully reminded that the examiner must examine a patent application according to the guidelines set forth by the USPTO as well as the MPEP, since the examiner has no authority to disregard such guidelines or to apply his own interpretation of patent law in the examination of the application. Furthermore, as set forth in the guidelines and the MPEP, the guidelines were promulgated by the USPTO in accordance with all applicable case law and thus are believed to be consistent therewith. While the examiner acknowledges the cited US patents, each patent application is examined on its own merits according to the current guidelines of examination as set forth by the USPTO and a discussion on the utility of any polynucleotide claimed in such patents would require a detailed review of the record of each individual case, which would be improper. Finally, applicants are further reminded that the examiner has no authority to comment in regard to the legality of the current utility guidelines or the MPEP as set forth by the USPTO.

It is noted that applicants separately address the enablement rejection of claims 1, 3-5, and 9-13 under 35 U.S.C. 112, first paragraph, at pages 19-20 of the response. Applicants argue that since the claimed invention has been "shown to have 'a specific, substantial, and credible utility,'" the enablement rejection under 35 U.S.C. 112, first paragraph, cannot stand. Applicants' argument is not found persuasive. In view of the reasons of record and the reasons stated above, there is no specific and substantial asserted utility or a well-established utility for the claimed invention and consequently, the enablement rejection of claims 1, 3-5, and 9-13 under 35 U.S.C. 112, first paragraph, is maintained.

[4] The written description rejection of claim 4 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record as set forth in item [10] of the Office action mailed January 9, 2004 and for the reasons stated below.

[5] RESPONSE TO ARGUMENTS: Applicants' arguments addressing the instant rejection begin at page 21 of the response. Applicants cite case law allegedly supporting a position that the specification adequately describes the claimed invention. Applicants argue that the claims at issue are in contrast to the claims of the Lilly and Fiers cases as the polynucleotides recited in the instant claims are not distinguished on the basis of function or a method of isolation, but are distinguished by structural features. Applicants argue that based on the sequences of the invention, one would be able to distinguish the claimed sequences from others based on the disclosed structural description. Applicants argue that nucleic acid molecules nucleotide sequences

encoding SEQ ID NO:4 are encompassed by the genus of claim 4 and those that lack this requirement are not. Applicants' arguments are not found persuasive.

It is acknowledged that the current claims differ from the Lilly and Fiers cases. However, applicants have failed to address the issue at hand – whether the specification discloses a *representative number of species* to adequately describe the genus of claimed polynucleotides. The written description requirement for a claimed genus may be satisfied through sufficient description of *a representative number of species* by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicants were in possession of the claimed genus. A representative number of species means that the species that are adequately described are representative of the entire genus. When there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. See MPEP § 2163. It is the examiner's position that the single disclosed representative species of SEQ ID NO:3 fails to adequately describe the claimed invention. As stated in a previous Office action (see page 10 of the Office action mailed June 09, 2003), SEQ ID NO:4 is only a fragment of a full-length polypeptide, and thus, the species encompassed by the genus of encoding nucleic acids of claim 4 reads on numerous undisclosed nucleic acids, including, *e.g.,* full-length genes, chromosomal DNA, and a variety of nucleic acids encoding proteins other than SEQ ID NO:4 or SEQ ID NO:2. In

the instant case, the claimed genus of polynucleotides encompasses species that are widely variant in both structure and function, including (but not limited to) genomic and chromosomal sequences from any organism comprising the recited sequence, allelic variants, and nucleic acid variants encoding polypeptides having function other than the activity of SEQ ID NO:2 (whatever that may be), e.g., non-functional polypeptides and polypeptides having activity other than the activity of SEQ ID NO:2. While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus", it is also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus". As the claimed genus encompasses species that are widely variant in both structure AND function, the disclosure of the single representative species of SEQ ID NO:3 is insufficient to be representative of the attributes and features of *all* species encompassed by the claimed genus of polynucleotides. In this case, applicants have failed to demonstrate that the specification discloses a representative number of species of the claimed genus of polynucleotides. Given the lack of description of a representative number of polynucleotides, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

Beginning at the bottom of page 21 of the response, applicants argue that because SEQ ID NO:4 is a fragment of SEQ ID NO:2, there are a large number of representative species that describe the claimed genus, SEQ ID NO:1 being such a

representative species. Applicants argue that any fragment of SEQ ID NO:1 that contains more than the first 4875 nucleotides of SEQ ID NO:1 is encompassed within the genus of claimed nucleic acids, asserting thus that the specification describes thousands of nucleic acids that would be encompassed within the genus. Applicants' argument is not found persuasive.

There is no dispute that SEQ ID NO:1 is encompassed within the genus of nucleic acids of claim 4. However, the genus is not so limited to SEQ ID NO:4 and SEQ ID NO:1. As admitted by applicants, there are thousands of nucleic acids encompassed within the genus. It is the examiner's position that the representative species of SEQ ID NO:4 and SEQ ID NO:1 fail to represent the entire genus of nucleic acids, which encompasses widely variant species, which is undisputed by applicant. It should be noted that, while the genus is limited by a structural feature that is present in all members of the genus, there is no correlation between this structural feature and the function of the nucleic acid. As such, the genus encompasses widely variant species having any function, including, inter alia, genomic DNA and nucleic acids encoding proteins having any function and the representative species of SEQ ID NO:1 and 4 fail to reflect the variation within the genus.

At the top of page 22 of the response, applicants "attempt a remedial explanation" as to how the examiner's arguments are directly in contrast with the relevant case law, are contradicted by the wealth of case law concerning claim scope, and are erroneous as asserted in applicants' previous response. Applicants argue that the examiner's assertion that "any variation within the genus... ...would arise due to the

addition of elements that are not part of the inventor's particular contribution" (quoting from page 10, middle of the Office action mailed June 09, 2003) is false. Applicants argue that the scope of claims 1 and 4 is not limited by the examiner's erroneous comments. Applicants' argument is not found persuasive.

The examiner is in full understanding of the meaning of the term "comprising" as a transitional phrase as set forth in MPEP 2111.03. It is noted that the examiner's remarks (as quoted by applicants) were directed at contrasting claims 1 and 4 and detailing why claim 1 was not rejected for written description under 35 USC 112, first paragraph. In this regard, the examiner maintains the position that claim 1 does not lack written description for those reasons set forth at page 10 of the Office action mailed June 09, 2003 and further, that these statements do not contradict case law. The examiner's determination that claim 4 lacks written description under 35 USC 112, first paragraph, was based on an analysis of the claims with respect to the Revised Interim Written Description Guidelines Training Materials, particularly Examples 7-8. It is noted that the language of the Office action found to be objectionable by applicants, i.e., "any variation within the genus... ...would arise due to the addition of elements that are not part of the inventor's particular contribution," can similarly be found at page 35, top of Example 8 of the Revised Interim Written Description Guidelines Training Materials, i.e., "any substantial variability within the genus arises due to addition of elements that are not part of the inventor's particular contribution."

[6] Status of claims:

- Claims 1-3 and 5-7 are pending in the application.

- Claims 1-3 and 5-7 are rejected.

- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:00 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for submission of official papers to Group 1600 is (703) 308-4242. Draft or informal FAX communications should be directed to (703) 746-5078. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman
Patent Examiner
Art Unit 1652
06-08-04